being replaced by a new situation where natural immunity is deferred until slightly older ages are reached.

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OVARIAN SURGERY WITH LOSS OF CORPUS LUTEUM IN EARLY PREGNANCY

REPORT OF TWO CASES BROUGHT TO TERM WITH PROGESTIN (DELALUTIN*) THERAPY

I. D. MacINTYRE, M.B., Ch.B., L.M.C.C., M.R.C.O.G., F.A.S.E.A.,† *Sarnia, Ont.*

The discovery of ovarian tumours in the pregnant patient is relatively uncommon but of potentially serious significance. Hesitation to perform the indicated pelvic laparotomy for fear of inducing abortion is likely to present a greater risk to fetal survival and maternal well-being than the operation itself.[1] The difficulty of accurate diagnosis of the nature of the mass, the frequency of malignant tumours, and the twisting of the affected ovary on its pedicle with necrosis or subsequent complication of delivery establish the need for early removal of solid or cystic neoplasm.[1-4] Dermoid cysts, which constitute approximately 10% of all ovarian tumours,[4] are particularly disposed to producing torsion of an ovary,[1] and immediate extirpation is imperative with the suspicion or diagnosis of a twisted dermoid. There are occasions when the encroachment of a cystic neoplasm or the finding of malignancy demands unilateral or bilateral oophorectomy or salpingo-oophorectomy with loss of the corpus luteum of pregnancy or all normally functioning ovarian tissue. Management of the patient under these conditions is an important factor in the eventual outcome of pregnancy.

When the corpus luteum is unavoidably lost in the early stages of gestation, the maintenance of adequate progestational activity to secure the continued growth and development of the fetus would appear to be indicated until placental support is well established. A postoperative program of progestin therapy can contribute to the preservation of pregnancy, complicated by cystectomy or oophorectomy within the first trimester, to a successful termination.[5-7] It is generally assumed that placental production of progesterone is initiated after approximately 90 days of pregnancy and that the dangers of abortion thereafter are not very substantial. In the interest of objectivity, however, it must be noted there are clinicians who believe that placental function begins much earlier in pregnancy and that there is little risk of spontaneous abortion even with the removal of the corpus luteum during the first trimester of gestation.[3] There are reports in the literature of patients who were carried to term following bilateral oophorectomy without the benefits of an exogenous supply of progestational hormone. Nevertheless these are presented as an unusual experience and it would be difficult to estimate from the literature the frequency with which pregnancy fails to survive this complication since abortion represents an anticipated consequence and is not likely to be reported. The administration of progestin to patients in early pregnancy is advocated as a precautionary measure which affords the fetus a maximum opportunity for survival.

Two cases are presented in this communication in which operation for removal of ovarian cysts entailed loss of the corpus luteum at approximately six weeks and at eight to 10 weeks of pregnancy. Postoperatively, the long-acting progestational agent, 17-alpha-hydroxyprogesterone caproate (Delalutin), was regularly administered for 2 to 2½ months when the fetal heart was clearly heard and pregnancy was found to be advancing normally. Supportive therapy was then discontinued. Unlike free progesterone, hydroxyprogesterone caproate may be given in relatively infrequent injections to simulate the action of the corpus luteum.[6, 8-10] Because of the prolonged biological activity of the ester, a schedule of daily injections to maintain adequate hormone levels is no longer necessary. While the 19-nortestosterone compounds employed for their progestational action have been found to exert a distinct androgenic effect,[8] implicating these substances as a possible cause of virilization of the

*Delalutin (17-alpha-hydroxyprogesterone-17-n-caproate) is a product of E. R. Squibb & Sons of Canada, Ltd.
†Sarnia General Hospital.

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fetus, hydroxyprogesterone caproate has not been associated with physical abnormalities in the female infant.[9] The present experiences indicate that the caproate compound is a convenient and potent source of progestational activity, protecting pregnancy at a critical stage in development and advancing it to the point where placental secretion of hormone was established, without adverse effects on the physical status of mother or infant.

Cystectomy with Excision of the Corpus Luteum

CASE 1.—The patient was 27 years old and gravida 2. She had not menstruated for two years prior to the present pregnancy but had successfully conceived and had been delivered of a normal child within this period. No difficulties were encountered during the earlier pregnancy or delivery. This time, however, having intimated that she considered herself pregnant again, she complained of severe pain confined to the right side of the abdomen. Pelvic examination showed the uterus to be enlarged to approximately the size of a six-week gestation. The cervix was soft and there was a mass in the right fornix which was extremely tender and suggestive of an extrauterine pregnancy. The enlargement of the uterus was considered compatible with that of an ectopic pregnancy.

The patient was admitted to hospital but her condition failed to improve. There was some element of shock, and a diagnosis of possible ectopic pregnancy was made with provision for immediate pelvic laparotomy. Operation established the presence of a cyst of the right ovary, 3.5 cm. in diameter, containing blood as well as a corpus luteum of pregnancy. The corpus luteum protruded into the cyst, communicating with it and extending partly into the ovary. It was impossible to save the corpus luteum of pregnancy and it was excised together with the cyst to which it was firmly attached.

Since the pregnancy was in its very early stages, progestin therapy was considered to be a judicious measure following operation. Initially, 125 mg. of hydroxyprogesterone caproate (Delalutin) was given by the intramuscular route daily for a period of seven days. Thereafter, injections were given every other day for seven days and then once weekly up to the fourth month of gestation. Throughout this time, the patient was well and there did not appear to be any disturbance of pregnancy. Progestin therapy was then discontinued.

Seven months after laparotomy, the patient was admitted to the hospital in early labour and was delivered on the following morning of a normal viable female infant, fully mature and weighing 6 lb. 4¼ oz. Delivery was effected with forceps because of transverse arrest with failure of the head to rotate and deliver itself spontaneously. The infant responded at once to resuscitation. According to the delivery date, the period of gestation was not prolonged by the hormone therapy nor did the infant appear to be unduly long or thin. Occasionally, when progesterone is given during pregnancy, the period of gestation may be prolonged somewhat or the infant appear thinner and longer than usual. Neither of these manifestations was present in this case and both mother and infant showed no adverse effects of a complicated pregnancy.

Oophorectomy for Removal of Bilateral Dermoid Cysts

CASE 2.—This patient, a white woman, 23 years of age, was first seen when she was six weeks' advanced in pregnancy. At that time she was well and pelvic examination confirmed the stage of gestation. At examination it was noted that the right ovary was larger than warranted by a normal corpus luteum of pregnancy and she was advised to report regularly for prenatal surveillance.

At approximately the tenth week of gestation, she complained of severe abdominal pain accompanied by nausea and vomiting. Her pulse rate was 100 beats per minute and her blood pressure was 86/40 mm. Hg. Careful examination failed to reveal the presence of intraperitoneal bleeding, and ectopic pregnancy was therefore considered unlikely. Pelvic examination indicated a large cystic mass in the cul-de-sac and in view of the previous pelvic findings, a diagnosis was made of ovarian cyst with torsion of the pedicle.

The patient was immediately hospitalized and laparotomy was undertaken the following day. The abdomen was opened through a mid-line, sub-umbilical incision. The uterus was delivered into the wound and was seen to be normal and in the eighth to tenth week of gestation. Both ovaries were cystic and impacted in the pouch of Douglas. The right ovary was completely replaced by cystic change and rotated one and one-half turns on its pedicle, with early resultant necrosis. The left ovary was similarly affected but retained a small portion of normal tissue in which was noted the corpus luteum of pregnancy. The cystic right ovary was completely removed. An attempt was made to exercise the cyst involving the left ovary. It was not possible to save the corpus luteum and this was also removed. The residual portion of ovarian tissue was less than 1 cm. in diameter and did not contain any luteal elements. No ovarian tissue was left on the right side.

Following operation, the patient was given a daily intramuscular injection of 125 mg. hydroxyprogesterone caproate (Delalutin) for six consecutive days. She made a good recovery and was allowed home seven days after operation. For the next month, she was given 125 mg. of the progestin twice weekly and the uterus continued to enlarge. Frequency of injection was then reduced to once weekly and after two weeks it was entirely discontinued when the fetal heart became audible. Pregnancy advanced uneventfully to term and the patient was delivered of a normal female infant seven months after operation. As in the previous case, the period of gestation was not prolonged by hormone treatment and the infant was normal in every respect. Neither mother nor infant exhibited adverse effects as a consequence of progestin therapy.

The ovarian tumours excised in this case were found to be dermoid cysts. There was no evidence of malignant involvement and the surgery and subsequent delivery were followed by complete recovery.

COMMENT

Until placental function is well established, the corpus luteum of pregnancy is the essential source of the progestational activity which sustains gestation and encourages the continued growth and development of the fetus. When emergency opera-

tion in the early stages of pregnancy entails an unavoidable loss of the corpus luteum, it seems a judicious precautionary measure to assure an exogenous supply of progestational hormone during the critical period prior to onset of placental production of progesterone. The use of free progesterone for this purpose is hampered by the need for daily injections and, on occasion, unusually high dosage to initiate and maintain satisfactory hormone levels. With the long-acting ester, 17-alpha-hydroxyprogesterone-17-n-caproate (Delalutin), intramuscular injection of 125 mg. daily during the first week after operation builds up a reservoir upon which the patient may draw so that subsequent treatment requires one or, at most, two injections weekly. When the fetal heart beat becomes audible, therapy may be discontinued. This program of progestin therapy has been found a satisfactory replacement for the lost corpus luteum hormones and has not produced adverse effects on the physical status of either mother or infant. Its use has not been associated with prolongation of the gestation period. Moreover, thus far, there have been no reports of an increased incidence of masculinization of the female infants born of mothers treated with hydroxyprogesterone caproate during pregnancy. The female infants of the patients described in this report were normal in all respects. For these reasons, hydroxyprogesterone caproate is considered a useful progestational agent for protection of pregnancy.

SUMMARY

Two cases are presented in which ovarian surgery with loss of the corpus luteum of pregnancy complicated the early stages of gestation. Both patients were brought to term with delivery of normal, viable, fully mature infants by the administration of progestin therapy in the critical postoperative period prior to the establishment of full placental function. The long-acting progestational agent, 17-alpha-hydroxyprogesterone-17-n-caproate (Delalutin) simulated corpus luteum activity, supporting gestation and stimulating the continued growth and development of the fetus pending placental assumption of progesterone production. There were no adverse effects of treatment on mother or infant. The usefulness of the caproate compound lies in its prolonged biological activity which enables the building up of a reservoir of progestational activity upon which the patient may draw as necessary. Maintenance of hormonal effects requires one or two injections weekly instead of the daily administrations which limit the efficiency of free progesterone.

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